

REMARKS

Claims 1-5, 7, 9, and 11-14 are pending in the instant application. Claims 1 and 13 have been amended. No new claims have been added and no new matter is introduced by the amendments to the previously presented claims. The amendment to Claim 1 is supported by paragraphs [0010] and [0032]-[0033] of the specification as filed, and the amendments to Claim 13 are formal in nature and merely correct a typographical error and clarify the antecedent basis for the recitation of “immature F1 embryos” as requested by the Examiner.

Objections to the Claims

The Examiner has objected to Claim 13 as informal due to the failure to recite “obtained from the F1 generation” after the recitation of “immature F1 embryos” in line 3. Applicants respectfully submit that the instant objection has been rendered moot in light of the amendment to Claim 13 presented above. Accordingly, Applicants request withdrawal of the instant objection.

Claims Rejections

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-5, 7, 9, and 11-14 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner contends that there is insufficient basis for the recitation “flanked by mobilizable sequence” in Claim 1. Claims 2-5, 7, 9, and 11-14 stand rejected as depending from a rejected claim. As outlined in the amendment to Claim 1, presented above, Applicants have removed the recitation of “flanked by” from the Claim. Applicants have replaced that recitation with the phrase

“bordered by.” The use of “bordered by” is supported by the following passages of the specification (emphasis added):

[0010] A subject of the present invention is therefore a method for obtaining a transgenic monocotyledon plant containing a gene of interest (i) free of foreign ancillary sequence comprising:

a) transforming at least one cell of a plant having no active transposase with a vector comprising two expression cassettes, one comprising a nucleotide sequence of interest (i), the other comprising a nucleotide sequence encoding a selection marker (ii) **bordered by the mobilizable sequences of a transposon**, said first expression cassette (comprising the nucleotide sequence of interest (i)) being outside the transposon element;

b) selecting the transformed plants with the selection marker (ii);

c) crossing a transformed plant with another plant belonging to a line containing in its genome a gene encoding an endogenous active transposase, and which is in the middle of a phenotypic marker for excision (iii), to obtain an F1 or any other individual of a subsequent generation;

d) selecting the cells or the individuals carrying the gene of interest free of foreign ancillary sequence, from the F1 generation;

e) regenerating plants from the cells or the individuals selected in (d).

and,

[0032] The marker gene to be eliminated (ii) **is integrated between two borders originating from the ends of an Ac element and containing the sequences required for transposition**. The complete construct is inserted into the T-DNA which thus carries a Ds-type defective transposon element containing the selection gene. This element is called Ds::M (M for selection Marker or phenotypic Marker).

[0033] The gene of interest is on the T-DNA and outside the Ds::M transposable element.

In light of the amendment to the claims, and the support for such amendments identified in the application as originally filed, Applicants respectfully request withdrawal of the instant rejection.

Rejections Under 35 U.S.C. § 103(a)

Claims 1-5, 7, 9, and 11-14 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Perez *et al.*, WO 98/38323, (hereinafter “Perez”) in view of Dellaporta *et al.*, Plenum Press, 263-282 (1998) (hereinafter “Dellaporta”), Ishida *et al.*, Nature Biotechnology, 14(6):745-750 (1996) (hereinafter “Ishida”), and Yoshida *et al.*, Journal of Bioscience and Bioengineering, 90:353-362 (2000) (hereinafter “Yoshida”).

In making the instant rejection the Examiner relies primarily on the teachings of Perez as outlining the claimed method. In particular, the Examiner contends that Perez teaches a method of obtaining a transgenic maize plant containing a coding sequence of interest, such as the AMS gene coding for male sterility, that is free of ancillary sequences. The Examiner supplements this teaching with the remainder of the cited art to argue that the application of the general methods disclosed in Perez could be extended to: (1) the use of the Ac transposase of the R-nj::Ac allele of the R-nj chromosome as a phenotypic marker of excision (based on Dellaporta); (2) the use of the maize line 188 (Ishida); and (3) the incorporation of a selection using GFP (based on Yoshida).

Although the Examiner suggests that Perez teach a method of obtaining a transgenic maize plant free of ancillary sequence, Applicants respectfully submit, as discussed in detail below, that the methods disclosed in Perez actually result in the retention of a fixed

transposase sequence as well as an antibiotic resistance gene in the final transgenic maize plants. The retention of such genes during the process of generating transgenic maize is exactly the disadvantage of earlier processes that is addressed by the instant invention. As outlined at paragraph [0004] of the instant application, using such methods “[selectable marker genes] remain in the plant and, consequently, can also be detected in the form of DNA or of proteins in certain derived products, whereas generally they do not provide any added value to the transformed plant obtained. The presence of these genes, and in particular the genes for resistance to antibiotics and herbicides, is today at the center of numerous debates regarding genetically modified organisms (Flavell et al., 1992; Chesson et al., 2000).” It is this concern over the introduction of antibiotic resistance (or other functional marker) genes into the wild that has created the desire to seek out alternatives to the strategies disclosed in Perez, such as the currently claimed method.

In describing the general method outlined in Perez, the Examiner points out that Perez begins by teaching the transformation of a first plant with a first T-DNA vector including the gene of interest followed by at least one selection sequence, such as nptII, and the appropriate regulatory sequences. Although the selection and regulatory sequences are flanked by mobilizable sequences responsive to a transposase, Perez note that the gene of interest is inserted outside of the mobilizable sequences and will thus be retained even if the sequence intervening the mobilizable sequences is excised (as outlined in Figure 1 of Perez).

The plant generated by this initial transformation is then crossed with a plant containing a transposase introduced into its genome using a second T-DNA vector (pBios144, which is described in detail in Figure 3). This second T-DNA vector is important in that it not only includes the left and right border T-DNA sequences necessary for introduction of the

transposase into the second plant's genome, but it also includes a nptII antibiotic resistance gene and a "fixed" transposase.¹ It is this fixed transposase that allows for the final step of the process.

The final step of the method described by Perez proceeds as follows:

- (1) The fixed transposase is expressed in a cell containing the transgenes provided both the first T-DNA vector and the second T-DNA vector;
- (2) The transposase introduced via the second T-DNA vector exerts its effects on the mobilizable sequences introduced via the first T-DNA vector;
- (3) The selection and regulatory sequences flanked by those mobilizable sequences are excised, but the gene of interest, which is not flanked by mobilizable sequences, is not excised.

Thus, the final step leaves the gene of interest without any associated ancillary sequence from that first T-DNA vector. However, as noted above, the transposase introduced by the second T-DNA vector is fixed and is incapable of excising itself. In addition, the nptII gene that was introduced along with the fixed transposase in the second T-DNA vector is also retained due to the lack of any mobilizable sequences flanking it. Accordingly, the method described in Perez involves the retention of a significant amount of ancillary sequence, including the particularly problematic antibiotic resistance gene.

In the instant Office Action the Examiner contends that it would have been obvious to one of skill in the art to replace the fixed transposase disclosed in Perez with the mobilizable transposase taught by Dellaporta. The Examiner contends that one of skill in the art would have been motivated to do so for the purpose of replacing a non-natural phenotypic

¹ A "fixed" transposase is one that is incapable of excising itself due to a mutation in one or both of its mobilizable sequences.

marker (GUS) for excision with a naturally occurring phenotypic marker (anthocyanin) as taught by Dellaporta.

The U.S. Patent and Trademark Office (“PTO”) published new guidelines on October 10, 2007, for Examiners to use in performing an obviousness analysis based on the recent U.S. Supreme Court decision in *KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007). Fed. Reg. 72:195, 57526-57535 (Oct. 10, 2007). The new guidelines state that PTO personnel must make the underlying factual inquiries required by *Graham v. John Deere Co.*: (1) determine the scope and content of the prior art; (2) ascertain the differences between the claimed invention and the prior art; and (3) resolve the level of ordinary skill in the art. In addition, the PTO guidelines also set forth seven specific rationales for rejecting claims as obvious based upon those underlying factual inquiries as well as the specific requirements that must be met to support a rejection under each rationale.

The Examiner’s rationales for the instant rejections are that one of ordinary skill in the art would have been motivated by the art itself to combine various aspects of Dellaporta, Ishida, and Yoshida to arrive at the instantly claimed invention. (See Pages 6-8 of the instant Office Action). In light of this language, the obviousness rejection appears to be based upon the rationale identified as “G. Some Teaching, Suggestion, or Motivation in the Prior Art That Would Have Led One of Ordinary Skill To Modify the Prior Art Reference or To Combine Prior Art Reference Teachings To Arrive at the Claimed Invention.” Fed. Reg. 72:195 at 57534. To support a rejection under this rationale, the guidelines note that it must be established that “one of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and that there would have been a reasonable expectation of success.” *Id.* Furthermore, the guidelines state that “if any of these findings cannot be made, then this

rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art.” Id.

Applicants respectfully submit that the references, alone or in combination, do not teach or suggest each and every feature of the pending claims, and therefore the suggested combination could not have “achieved the claimed invention” as required by the PTO’s own obviousness guidelines and the prevailing case law. Id.; In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). In particular, Applicants note that the method described by Perez does not result in the removal of all ancillary sequence, due to the use of second T-DNA vector that introduces both a fixed transposase and an antibiotic resistance gene (nptIII) that are not flanked by mobilizable sequences. This retention of ancillary sequence would not be cured even if the proposed combination with Dellaporta was permitted. Specifically, Applicants note that Figure 3 of Perez indicates the presence of an nptIII gene that is not bordered by mobilizable sequence and thus would not be removed even if an active Ac element from a R-nj::AC allele of the R-nj chromosomal locus was used. The Examiner’s comments in the instant Office Action do not address the presence of this nptIII gene, nor how that gene would be removed upon combination of Perez with Dellaporta. Given these differences from the claimed invention, and the fact that neither Ishida nor Yoshida provide sufficient teaching to supplement the deficiency identified in Perez, Applicants respectfully request withdrawal of the instant rejection.

Applicants also submit that the Examiner is engaging in impermissible hindsight and using the instant application as a roadmap in an attempt to string together the various references to arrive at the instant invention. As outlined by the Federal Circuit,

[i]n making the assessment of differences, section 103 specifically requires consideration of the claimed invention “as a whole.” Inventions typically are new combinations of existing principles or features. The “as

a whole” instruction in Title 35 prevents evaluation of the invention part by part. Without this important requirement, an obviousness assessment might break an invention into its component parts (A+B+C), then find a prior art reference containing A, another containing B, and another containing C, and on that basis alone declare the invention obvious. **This form of hindsight reasoning, using the invention as a roadmap to find its prior art components, would discount the value of combining various existing features or principles in a new way to achieve a new result - often the very definition of invention.**²

In the instant situation, the Examiner argues that the motivation for combining Perez with Dellaporta is for the purpose of replacing a non-natural phenotypic marker for excision with a naturally occurring phenotypic marker. The Examiner does not identify any suggestion of this motivation in either Perez or Dellaporta. Instead, this motivation appears to have been derived entirely from the teachings of the instant application, particularly paragraph [0004], which is detailed above. Given that the motivation must appear in the cited references, and not lifted from the application under examination, Applicants respectfully submit that the Examiner has not established a *prima facie* case for obviousness and request that the instant rejection be withdrawn.

² See *Ruiz v. A.B. Chance Co.*, 69 USPQ2d 1686, 1690 (Fed Cir 2004), internal citations deleted, emphasis added.

Conclusion

Entry of the foregoing amendments and remarks into the file of the above-identified application is respectfully requested. An early allowance is earnestly sought. To expedite allowance of this application, the Examiner is invited to telephone the undersigned if the Examiner believes a telephone call would be helpful in advancing prosecution.

Respectfully submitted,



Steve Lendaris
PTO Reg. No. 53,202
Attorneys for Applicants
BAKER BOTTS L.L.P.
30 Rockefeller Plaza
New York, NY 10112--4498
(212) 408-2500